UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,261	12/03/2003	Herbert W. Harris	18184-0004 US	7783

23973 7590 12/16/2008

DRINKER BIDDLE & REATH
ATTN: INTELLECTUAL PROPERTY GROUP
ONE LOGAN SQUARE
18TH AND CHERRY STREETS
PHILADELPHIA, PA 19103-6996

EXAMINER	
CARTER, KENDRA D	
ART UNIT	**PAPER NUMBER**
1617	

MAIL DATE	DELIVERY MODE
12/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/728,261	HARRIS ET AL.	
	Examiner	Art Unit	
	KENDRA D. CARTER	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-12* is/are allowed.

6)☒ Claim(s) *13-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner acknowledges the applicant's remarks and arguments of August 15, 2008 made to the office action filled May 2, 2008. Claims 1-58 are pending.

In light of the terminal disclaimer filed August 15, 2008, the nonstatutory obviousness-type double patenting rejection of claims 1-12 as being unpatentable over claims 1, 10-14, and 16-20 of copending Application No. 10/578,522, is withdrawn.

Allowable Subject Matter

Claims 1-12 are allowed.

Election/Restrictions

The restriction requirement filed May 17, 2006, has been reconsidered in view of the allowability of claims to the elected invention pursuant to MPEP § 821.04(a). **The restriction requirement is hereby withdrawn as to any claim that requires all the limitations of an allowable claim.** Claims 13-58, are directed to the methods of using the composition are no longer withdrawn from consideration because the claim(s) requires all the limitations of an allowable claim.

In view of the above noted withdrawal of the restriction requirement, applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Once a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

1) Claims 13-17 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 5 and 7-12 of prior U.S. Patent No. 6,864,251 B2. This is a double patenting rejection.

2) Claims 13, 17 and 18 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 12 of prior U.S. Patent No. 6,638,928 B1. This is a double patenting rejection.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3) Claims 13-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 7, 8, 14, 16 and 20 of U.S.

Application No. 10/578,522. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The US Application No. 10/578,522 teaches the treatment of inflammatory disorder of epithelial tissue such as skin disorder and gastrointestinal disorders with the applicants compound in its racemic mixture or in the (R)-enantiomer substantially free of the corresponding (S)-enantiomer.

The US Application No. 10/578,522 does not specifically teach the treatment of psoriasis, inflammatory bowel disease, Crohn's Disease or radiation induced gastrointestinal inflammation. The application 10/578,522 also does not specifically teach the specific amounts of the (R)-enantiomer that are present in the composition as in the present application claims 2, 7 and 12.

To one of ordinary skill in the art it would be obvious to treat psoriasis, inflammatory bowel disease, Crohn's Disease or radiation induced gastrointestinal inflammation because they are all either an inflammatory disorder of epithelial tissue such as skin disorder and gastrointestinal disorders. Further, the specific amounts of the (R)-enantiomer would be obvious because one skilled in the art can adjust the amount of the enantiomer based on common skill.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1) Claims 13-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are drawn to a method of treating, preventing, or the delaying the onset of a leukotriene B_4-mediated inflammatory disorder. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art;

(6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 13 is drawn to "a method of treating an leukotriene B_4-mediated inflammatory disorder in an individual in need of such treatment, comprising administering to said individual a therapeutically effective amount of a composition according to claim 1." The claim 17 is drawn to "the method of claim 13 wherein the disorder is selected from the group consisting of inflammatory bowel disease, ulcerative colitis, psoriasis, rheumatoid arthritis, Crohn's Disease and radiation induced gastrointestinal inflammation." Claim 18 is drawn to "a method of preventing or delaying the onset of an inflammatory disorder mediated by leukotriene B_4 in an individual who is at risk of developing an inflammatory disease state, said method comprising administering to said individual a therapeutically effective amount of the composition according to claim 1."

(2) The breadth of the claims:

Claims 13-21 embraces treating, preventing or delaying the onset of <u>any</u> inflammatory disorder mediated by leukotriene B_4. This reads on treating, preventing or delaying the onset of <u>all</u> inflammatory disorders associated with leukotriene B_4. The specification <u>does not</u> enable the treatment, prevention or delaying the onset of <u>any</u> inflammatory disorder mediated by leukotriene B_4.

(3) The state of the prior art:

The state of the art regarding preventing treating, preventing or delaying the onset of all inflammatory disorders associated with leukotriene B_4 is very low or do not exist. Riccioni et al. (Annals of Clinical and Laboratory Science, 2004, vol. 34, no. 4, pp. 379-387) teaches that leukotrienes have been successful for asthma management and are being considered as new applications for new applications such as the treatment of chronic urticaria, atopic dermatitis, chronic obstructive pulmonary disease, interstitial cystitis and irritable bowel syndrome. Although double-blind, randomized, placebo-controlled trials are needed to confirm the effects that these drugs may have in these diseases (see abstract). For instance, in chronic urticaria, leukotriene might be effective if combined with another drug (see page 381, chronic urticaria, last 6 lines). Thus, drugs must be tested with each condition to see if the particular leukotriene inhibitor is effective. In this case, the Applicant's claimed compound has been shown to inhibit leukotriene B_4 but has not been shown to be effectively treat any of vast number of disorders associated with leukotriene B_4.

(4) The predictability or unpredictability of the art:

The predictability of treating, preventing or delaying the onset of all inflammatory disorders associated with leukotriene B_4 is relatively low. As taught by Riccioni et al. double-blind, randomized, placebo-controled trials are needed to confirm that antileukotriene drugs are even effective. Therefore, to one skilled in the art, treating,

preventing or delaying the onset of all inflammatory disorders associated with leukotriene B_4 is highly unpredictable.

(5) The relative skill of those in the art:

The relative skill of those in the art is high as demonstrated by Riccioni et al.

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to the treating, preventing or delaying the onset of all inflammatory disorders associated with leukotriene B_4 is completely lacking. The specification as filed does not speak on or show any working examples any studies performed that treat, prevent, or delay the onset of all inflammatory disorders associated with leukotriene B_4. On page 45 of the specification, the Applicant demonstrated that the claimed compound binds to the LTB_4 receptor, but does not demonstrate the compound effectively treats any of the vast amount of disorders that are associated with the binding of the LTB_4 receptor. As taught by Riccioni et al., although known leukotriene inhibitors are known and have been tested to treat several disorders associated with the leukotriene pathway does not mean that it is effective in treating the particular disorder. If anything, Riccioni et al. gives motivation to try other leukotriene inhibitors to see if they are effective in disorders other than asthma, but does not in any way suggest that all leukotriene inhibitors are effective to treat all inflammatory disorders associated with inhibiting leukotriene. Note that lack of a

working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02.

(7) The quantity of experimentation necessary:

The instant claims read treating, preventing or delaying the onset of all inflammatory disorders associated with leukotriene B_4. As discussed above the specification fails to provide any support for effectively treating, preventing or delaying the onset of any inflammatory disorders associated with leukotriene B_4. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F. 3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable.

In conclusion, the applicant is enabled for inhibiting LTB_4 with the claim compound, but not for treating, preventing or delaying the onset of all or any inflammatory disorders associated with leukotriene B_4.

2) Claims 22-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are drawn to a method of treating, preventing, or the delaying the onset of a thromboxan A_2-mediated disorder. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 22 is drawn to "a method of treating thromboxan A_2-mediated disorder in an individual in need of such treatment, comprising administering to said individual a therapeutically effective amount of a composition according to claim 1." The claim 27 is drawn to "the method of claim 26 wherein the chronic inflammatory disorder is selected from the group consisting of chronic fatigue syndrome/fibromyalgia, infertility, osteonecrosis of the jaw, multiple sclerosis, depression, autism, Crohn's Disease, Inflammatory Bowel Disease, late Lyme Disease, Sjogren's Syndrome, transient ischemic attack, attention deficit disorder and Parkinson's Disease." Claim 32 is drawn

to "a method of preventing or delaying the onset of a thromboxan A_2-mediated disorder in an individual in need of such treatment, comprising administering to said individual a therapeutically effective amount of the composition according to claim 1."

(2) The breadth of the claims:

Claims 22-32 embraces treating, preventing or delaying the onset of any thromboxan A_2-mediated disorder. This reads on treating, preventing or delaying the onset of all thromboxan A_2-mediated disorders. The specification does not enable the treatment, prevention or delaying the onset of any thromboxan A_2-mediated disorder.

(3) The state of the prior art:

The state of the art regarding preventing treating, preventing or delaying the onset of all thromboxan A_2-mediated disorders is very low or do not exist. Vermylen et al. (Cardiovascular Drugs and Therapy, 1992, vol. 6, pp. 29-33) teaches that a first sight a thromboxan sythase inhibitor (TSI) presents some major advantages such as selectively inhibiting TXA_2 formation, but despite its interesting properties, the first clinical trials with TSI have been disappointing (see page 30, column 2, thrombaxan synthase inhibitors in its entirety).

(4) The predictability or unpredictability of the art:

The predictability of treating, preventing or delaying the onset of all thromboxan A_2-mediated disorders is relatively low. As taught by Vermylen et al. first clinical trials

with TSI have been disappointing (see page 30, column 2, thrombaxan synthase inhibitors, third paragraph, lines 1-2). Therefore, to one skilled in the art, treating, preventing or delaying the onset of all thromboxan A_2-mediated disorders is highly unpredictable.

(5) The relative skill of those in the art:

The relative skill of those in the art is high as demonstrated by Vermylen et al.

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to the treating, preventing or delaying the onset of all thromboxan A_2-mediated disorders is completely lacking. The specification as filed does not speak on or show any working examples any studies performed that treat, prevent, or delay the onset of all or any thromboxan A_2-mediated disorder. On page 46 of the specification, the Applicant demonstrated that the claimed compound binds to the TXA_2 receptor and demonstrates a 48.26% inhibition, but does not demonstrate the compound effectively treats any of the vast amount of disorders that are associated with the binding of the TXA_2 receptor. As taught by Vermylen et al., thromboxan sythase inhibitor (TSI) presents some major advantages such as selectively inhibiting TXA_2 formation, but despite its interesting properties, the first clinical trials with TSI have been disappointing (see page 30, column 2, thrombaxan synthase inhibitors in its entirety). Thus, one skilled in the art is not enabled from the Applicant's specification to effectively treat any thromboxan A_2-mediated disorder because prior art teaches that

thromboxan sythase inhibitors in general have been disappointing in regards to therapy. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02.

(7) The quantity of experimentation necessary:

The instant claims read treating, preventing or delaying the onset of all thromboxan A_2-mediated disorders. As discussed above the specification fails to provide any support for effectively treating, preventing or delaying the onset of any thromboxan A_2-mediated disorder. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F. 3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable. One skilled in the art would need to first establish that the Applicant's claimed compounds is actually effective in treated, preventing or delaying the onset of any thromboxan A_2-mediated disorder.

In conclusion, the applicant is enabled for inhibiting TXA_2 with the claimed compound, but not for treating, preventing or delaying the onset of all or any thromboxan A_2-mediated disorder.

3) Claims 33-53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are drawn to a method of treating an adenosine-mediated disorder. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 33 is drawn to "a method of treating an adenosine-mediated disorder in an individual in need of such treatment, comprising administering to said individual a therapeutically effective amount of a composition according to claim 1." The claim 37 is

drawn to “the method of according to claim 33 wherein the disorder mediated by adenosine is a central nervous system disorder associated with elevated electrical excitability of neurons." The claim 39 is drawn to “the method of according to claim 33 wherein the disorder mediated by adenosine is a central nervous system disorder associated with decreased cerebral blood flow.” Claim 40 is drawn to “the method of according to claim 33 wherein the disorder mediated by adenosine is a central nervous system disorder associated with increased release of excitatory amino acids.” Claim 43 is drawn to “the method of according to claim 33 wherein the disorder mediated by adenosine is neuronal cell death associated with adenosine mediated cerebral ischemia or stroke.” Claim 44 is drawn to “the method according to claim 33 wherein the disorder mediated by adenosine is migraine." Claim 45 is drawn to “the method according to claim 33 wherein the disorder mediated by adenosine is Parkinson’s Disease." Claim 46 is drawn to “the method according to claim 33 wherein the disorder mediated by adenosine is congestive heart failure." Claim 47 is drawn to “the method according to claim 33 wherein the disorder mediated by adenosine is coronary artery disease." Claim 48 is drawn to “the method according to claim 33 wherein the disorder mediated by adenosine is hypertension." Claim 49 is drawn to “the method according to claim 33 wherein the disorder mediated by adenosine is renal failure." Claim 50 is drawn to “the method according to claim 33 wherein the disorder mediated by adenosine is glaucoma." Claim 51 is drawn to “the method according to claim 33 wherein the disorder mediated by adenosine is asthma." Claim 52 is drawn to “the method according to claim 33 wherein the disorder mediated by adenosine is myelosuppression

associated with cytotoxic chemotherapy or ionizing radiation therapy." Claim 53 is drawn to "the method according to claim 33 wherein the disorder mediated by adenosine is a chronic inflammatory disorder."

(2) The breadth of the claims:

Claims 33-53 embraces and reads on treating any adenosine-mediated disorder. The specification does not enable the treatment any adenosine-mediated disorder.

(3) The state of the prior art:

The state of the art regarding preventing treating all adenosine-mediated disorder is very low or do not exist. Gomtsyan et al. (Current Pharmaceutical Design, 2004, vol. 10, pp. 1093-1103) teach that adenosine kinase inhibitors have been shown to provide effective antinociceptive, anti-inflammatory and anti-convulsant activity in animal modes, thus suggesting their potential therapeutic utility for pain, inflammation epilepsy and possibly other central and peripheral nervous system disease associated with cellular trauma and inflammation (see abstract, lines 5-8). There has been two attempt to develop nucleoside-like adenosine kinase inhibitors as therapeutics, in which one gave undisclosed results and the other was halted due to an apparent increase in the incidence of CNS hemorrhage in rats and dogs. Whether this finding is a chemical class specific phenomenon which nonnucleoside adenosine kinase inhibitors have potential to overcome, remains to be investigated (see page 1101, column 1, last 9 lines). Thus, all adenosine kinase inhibitors are not effective to treat all disorders

associated with adenosine. Further, Terasaka (Expert Opinon of Therapeutic Patents, vol. 15, no. 7, July 1, 2005) teaches that most adenosine inhibitors to date are purine nuclesides or alkyladenine analogues that have poor pharmacokinetics and/or several toxicities. Adenosine inhibitors without these problems may improve the treatment of leukaemia and also have potential for use in many other clinical conditions. This hypothesis has generated considerable interest in the development of non-nucleoside adenosine inhibitors (see abstract). Thus, each potential adenosine inhibitor, including those with alkyladeneine analogues need to be tested for efficacy. In other words, just because a compound inhibits adenosine does not mean that the compound is effective in treating all or any adenosine mediated disorder.

(4) The predictability or unpredictability of the art:

The predictability of treating all or any adenosine-mediated disorder is relatively low. As taught by Gomtsyan et al. and Terasaka just because a compound inhibits adenosine does not mean that the compound is effective in treating all or any adenosine mediated disorder. Therefore, to one skilled in the art, treating all adenosine-mediated disorders with any adenosine inhibitor is highly unpredictable.

(5) The relative skill of those in the art:

The relative skill of those in the art is high as demonstrated by Gomtsyan et al. and Terasaka.

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to the treating all or any adenosine-mediated disorder is completely lacking. The specification as filed does not speak on or show any working examples any studies performed that treat any thromboxan A_2-mediated disorder. On page 46 of the specification, the Applicant demonstrated that the claimed compound binds demonstrated 61.50% inhibition at the adenosine receptor, but does not demonstrate the compound effectively treats any of the vast amount of disorders that are associated with inhibiting the adenosine receptor. As taught by Gomtsyan et al. and Terasaka, just because a compound inhibits adenosine does not mean that the compound is effective in treating all or any adenosine mediated disorder. Thus, one skilled in the art is not enabled from the Applicant's specification to effectively treat any adenosine-mediated disorder because prior art teaches that adenosine inhibitors in general are not effective to treat adenosine-mediated disorders. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02.

(7) The quantity of experimentation necessary:

The instant claims read treating all adenosine-mediated disorders. As discussed above the specification fails to provide any support for effectively treating any adenosine-mediated disorder. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F. 3d at

1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable. One skilled in the art would need to first establish that the Applicant's claimed compounds is actually effective in treated any adenosine-mediated disorder.

In conclusion, the applicant is enabled for inhibiting binding at the adenosine receptor with the claimed compound, but not for treating any adenosine-mediated disorder.

4) Claims 54 and 55 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are drawn to a method of enhancing wound healing. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 54 is drawn to “a method of enhancing wound healing, said method comprising administering to said individual a therapeutically effective amount of a composition according to claim 1.” The claim 55 is drawn to “a method according to claim 54 of enhancing wound healing in advance of a surgical procedure."

(2) The breadth of the claims:

Claims 54 and 55 embrace and read on enhancing wound healing. The specification does not enable the enhancement of wound healing.

(3) The state of the prior art:

The state of the art regarding enhancing wound healing with the claimed compound does not exist. The specification has found that the claimed compound inhibits TXA2, LTB_4 and adenosine (see page 47, table 2). The specification teaches that adenosine A_1 receptor provides wound healing (see page 15, table 1). As discussed in the above 35 US 112 rejections and repeated below, the prior art does not enable these type compounds, or inhibitors of adenosine receptors in general to

enhance wound healings. Gomtsyan et al. (Current Pharmaceutical Design, 2004, vol. 10, pp. 1093-1103) teach that adenosine kinase inhibitors have been shown to provide effective antinociceptive, anti-inflammatory and anti-convulsant activity in animal modes, thus suggesting their potential therapeutic utility for pain, inflammation epilepsy and possibly other central and peripheral nervous system disease associated with cellular trauma and inflammation (see abstract, lines 5-8). There has been two attempt to develop nucleoside-like adenosine kinase inhibitors as therapeutics, in which one gave undisclosed results and the other was halted due to an apparent increase in the incidence of CNS hemorrhage in rats and dogs. Whether this finding is a chemical class specific phenomenon which nonnucleoside adenosine kinase inhibitors have potential to overcome, remains to be investigated (see page 1101, column 1, last 9 lines). Thus, all adenosine kinase inhibitors are not effective to treat all disorders associated with adenosine. Further, Terasaka (Expert Opinon of Therapeutic Patents, vol. 15, no. 7, July 1, 2005) teaches that most adenosine inhibitors to date are purine nuclesides or alkyladenine analogues that have poor pharmacokinetics and/or several toxicities. Adenosine inhibitors without these problems may improve the treatment of leukaemia and also have potential for use in many other clinical conditions. This hypothesis has generated considerable interest in the development of non-nucleoside adenosine inhibitors (see abstract). Thus, each potential adenosine inhibitor, including those with alkyladeneine analogues need to be tested for efficacy. In other words, just because a compound inhibits adenosine does not mean that the compound is effective in treating all or any adenosine mediated disorder. Lastly, the applicant has found that

the claimed compound is nonselective in inhibiting adenosine (see page 46 and 47, table 2). Thus, since the A_1 and A_{2B} receptors subtypes (see specification, page 15, table 1) are responsible for wound healing, there is no evidence that the Applicant's compound will be effective to bind to these receptors more than the other receptor subtypes such as A_{2B} and A_3.

(4) The predictability or unpredictability of the art:

The predictability of enhancing wound healing is relatively low. As taught by Gomtsyan et al. and Terasaka just because a compound inhibits adenosine does not mean that the compound is effective in treating all or any adenosine mediated disorder. Therefore, to one skilled in the art, treating enhancing wound healing with any adenosine inhibitor is highly unpredictable. One skilled in the art would need to determine if the compound is effective.

(5) The relative skill of those in the art:

The relative skill of those in the art is high as demonstrated by Gomtsyan et al. and Terasaka.

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to the treating enhancing wound healing is completely lacking. The specification as filed does not speak on or show any working examples any studies performed that enhance wound healing. On

page 15, table 1, of the specification, the Applicant teaches that adenosine receptors A_1 and A_{2A} are responsible for wound healing. The Applicant's also demonstrated that the claimed compound binds demonstrated 61.50% inhibition at the adenosine receptor, but does not demonstrate the compound effectively enhances wound healing or specifically binds to the respective receptors responsible for wound healing versus the other receptor subtypes. As taught by Gomtsyan et al. and Terasaka, just because a compound inhibits adenosine does not mean that the compound is effective in treating all or any adenosine mediated disorder. Thus, one skilled in the art is not enabled from the Applicant's specification to effectively enhance wound healing because prior art teaches that adenosine inhibitors in general are not effective to treat adenosine-mediated disorders. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02.

(7) The quantity of experimentation necessary:

The instant claims read enhancing wound healing. As discussed above the specification fails to provide any support for effectively enhancing wound healing. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F. 3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable.

One skilled in the art would need to first establish that the Applicant's claimed compounds is actually effective in enhancing wound healing.

In conclusion, the applicant is enabled for inhibiting binding at the adenosine receptor with the claimed compound, but not for enhancing wound healing.

5) Claims 56 and 57 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are drawn to a method of inducing gastrointestinal relaxation in an individual, particularly an individual suffering from irritable bowel syndrome. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:
(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 56 is drawn to “a method of inducing gastrointestinal relaxation in an individual in need of such treatment, said method comprising administering to said individual a therapeutically effective amount of a composition according to claim 1.” The claim 57 is drawn to “a method according to claim 56 wherein said individual is suffering from irritable bowel syndrome."

(2) The breadth of the claims:

Claims 56 and 57 embrace and read on inducing gastrointestinal relaxation in an individual. The specification does not enable inducing gastrointestinal relaxation in an individual.

(3) The state of the prior art:

The state of the art regarding inducing gastrointestinal relaxation in an individual with the claimed compound does not exist. The specification has found that the claimed compound inhibits TXA2, LTB_4 and adenosine (see page 47, table 2). The specification teaches that TXA2 agents may be useful for treating inflammatory bowel disease (see page 13, paragraph 1) and that LTB_4 is associated with inflammatory bowel disease (see page 5, second paragraph). As discussed in the above 35 US 112 rejections and repeated below, the prior art does not enable these type compounds, or inhibitors of TXA2 and LTB_4 in general to induce gastrointestinal relaxation, particularly irritable

bowel syndrome. Riccioni et al. (Annals of Clinical and Laboratory Science, 2004, vol. 34, no. 4, pp. 379-387) teaches that leukotrienes have been successful for asthma management and are being considered as new applications for new applications such as the treatment of chronic urticaria, atopic dermatitis, chronic obstructive pulmonary disease, interstitial cystitis and irritable bowel syndrome. Although double-blind, randomized, placebo-controlled trials are needed to confirm the effects that these drugs may have in these diseases (see abstract). There have been limited studies in which there have been beneficial effects of the leukotriene inhibitor montelukast with IBS (see page 383 column 1, irritable bowel syndrome). The beneficial results of montelukast do not suggest that all leukotriene inhibitors will act the same because as Riccioni et al. teaches that the compounds are being considered and further testing is needed. Thus, Riccioni et al. invites one skilled in the art to test other leukotriene inhibitors to treat IBS, but does not suggest that all inhibitors of any chemical structure will provide effective treatment of IBS.

Further, Vermylen et al. (Cardiovascular Drugs and Therapy, 1992, vol. 6, pp. 29-33) teaches that a first sight a thromboxan sythase inhibitor (TSI) presents some major advantages such as selectively inhibiting TXA_2 formation, but despite its interesting properties, the first clinical trials with TSI have been disappointing (see page 30, column 2, thrombaxan synthase inhibitors in its entirety). Thus, it is not well known in the art that thromboxan inhibitors in general treat IBS.

(4) The predictability or unpredictability of the art:

The predictability of inducing gastrointestinal relaxation in an individual, particularly an individual suffering from irritable bowel syndrome is relatively low. As taught by Riccioni et al. and Vermylen et al. just because a compound inhibits leukotriene or thromboxan does not mean that the compound is effective in treating IBS. Therefore, to one skilled in the art, inducing gastrointestinal relaxation in an individual, particularly an individual suffering from irritable bowel syndrome with any leukotriene or thromboxan inhibitor is highly unpredictable. One skilled in the art would need to determine if the compound is effective.

(5) The relative skill of those in the art:

The relative skill of those in the art is high as demonstrated by Riccioni et al. and Vermylen et al.

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to inducing gastrointestinal relaxation in an individual, particularly an individual suffering from irritable bowel syndrome is completely lacking. The specification as filed does not speak on or show any working examples any studies performed that induce gastrointestinal relaxation in an individual, particularly an individual suffering from irritable bowel syndrome. The specification teaches that TXA2 agents may be useful for treating inflammatory bowel disease (see page 13, paragraph 1) and that LTB_4 is associated with inflammatory bowel disease (see page 5, second paragraph). Futher,

the specification teaches that the claimed compound inhibits TXA2 and LTB_4 on page 47, table 2, but does not demonstrate the compound effectively induce gastrointestinal relaxation. As Riccioni et al. only invites one skilled in the art to test other leukotriene inhibitors to treat IBS, Ricconi et al. does not suggest that all inhibitors of any chemical structure will provide effective treatment of IBS. Further, Vermylen et al. provides teaching that it is not well known in the art that thromboxan inhibitors in general treat IBS. Thus, one skilled in the art is not enabled from the Applicant's specification to effectively induce gastrointestinal relaxation because prior art teaches that leukotriene and thromboxan inhibitors in general are not effective to treat disorders such as IBS. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02.

(7) The quantity of experimentation necessary:

The instant claims read inducing gastrointestinal relaxation. As discussed above the specification fails to provide any support for effectively inducing gastrointestinal relaxation. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F. 3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable. One skilled in the art would need to first establish that the Applicant's claimed compounds is actually effective in inducing gastrointestinal relaxation.

In conclusion, the applicant is enabled for inhibiting TXA2 and LTB_4 with the claimed compound, but not for inducing gastrointestinal relaxation.

6) Claim 58 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are drawn to a method of preventing, reducing or delaying the onset of myelosuppression associated with cytotoxic chemotherapy or ionizing radiation therapy. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:
(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 58 is drawn to "a method a method of preventing, reducing or delaying the onset of myelosuppression associated with cytotoxic chemotherapy or ionizing radiation therapy in an individual who is at risk of developing such myelosuppression due to the present or imminent administration to said individual of cytotoxic chemotherapy or ionizing radiation therapy, said method comprising administering to said individual a therapeutically effective amount of a composition according to claim 1."

(2) The breadth of the claims:

Claim 58 preventing, reducing or delaying the onset of myelosuppression associated with cytotoxic chemotherapy or ionizing radiation therapy. The specification does not enable preventing, reducing or delaying the onset of myelosuppression associated with cytotoxic chemotherapy or ionizing radiation therapy.

(3) The state of the prior art:

The state of the art regarding preventing, reducing or delaying the onset of myelosuppression associated with cytotoxic chemotherapy or ionizing radiation therapy is very low or do not exist. In the specification on page 17, the Applicant's disclose that adenosine has been investigated as a potential mediator in regeneration of hemotopoietic progenitor cells in mouse models of severe myelosuppression. The tests were administered in a 4-day treatment regimen starting on day 3 after induction of myuelosuppression. The drug significantly elevated numbers of granulocytes and less pronounced elevation of lymphocytes and erythrocytes. Thus, although this study

demonstrates possible treatment, it does not provide enablement for all adenosine inhibitors, nor the prevention of myelosuppression. In other words, the study provides one skilled in the art motivation to try other adenosine inhibitors, but does not indicate that all adenosine inhibitors are effective in preventing, reducing or delaying the onset of myelosuppression.

Further, Gomtsyan et al. (Current Pharmaceutical Design, 2004, vol. 10, pp. 1093-1103) teach that adenosine kinase inhibitors have been shown to provide effective antinociceptive, anti-inflammatory and anti-covulsant activity in animal modes, thus suggesting their potential therapeutic utility for pain, inflammation epilepsy and possibly other central and peripheral nervous system disease associated with cellular trauma and inflammation (see abstract, lines 5-8). There has been two attempt to develop nucleoside-like adenosine kinase inhibitors as therapeutics, in which one gave undisclosed results and the other was halted due to an apparent increase in the incidence of CNS hemorrhage in rats and dogs. Whether this finding is a chemical class specific phenomenon which nonnucleoside adenosine kinase inhibitors have potential to overcome, remains to be investigated (see page 1101, column 1, last 9 lines). Thus, all adenosine kinase inhibitors are not effective to treat all disorders associated with adenosine.

Lastly, Terasaka (Expert Opinon of Therapeutic Patents, vol. 15, no. 7, July 1, 2005) teaches that most adenosine inhibitors to date are purine nuclesides or alkyladenine analogues that have poor pharmocokinetics and/or several toxicities. Adenosine inhibitors without these problems may improve the treatment of leukaemia

and also have potential for use in many other clinical conditions. This hypothesis has generated considerable interest in the development of non-nucleoside adenosine inhibitors (see abstract). Thus, each potential adenosine inhibitor, including those with alkyladeneine analogues need to be tested for efficacy. In other words, just because a compound inhibits adenosine does not mean that the compound is effective in treating all or any adenosine mediated disorder, particularly myelosuppression.

(4) The predictability or unpredictability of the art:

The predictability of preventing, reducing or delaying the onset of myelosuppression associated with cytotoxic chemotherapy or ionizing radiation therapy is relatively low. As taught by Gomtsyan et al. and Terasaka just because a compound inhibits adenosine does not mean that the compound is effective in treating all or any adenosine mediated disorder. Therefore, to one skilled in the art, preventing, reducing or delaying the onset of myelosuppression associated with cytotoxic chemotherapy or ionizing radiation therapy is highly unpredictable.

(5) The relative skill of those in the art:

The relative skill of those in the art is high as demonstrated by Applicant's teaching on page 17 of the specification, Gomtsyan et al. and Terasaka.

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to preventing, reducing or delaying the onset of myelosuppression associated with cytotoxic chemotherapy or ionizing radiation therapy is completely lacking. The specification as filed does not speak on or show any working examples any studies performed that treat preventing, reducing or delaying the onset of myelosuppression associated with cytotoxic chemotherapy or ionizing radiation therapy. On page 46 of the specification, the Applicant demonstrated that the claimed compound binds demonstrated 61.50% inhibition at the adenosine receptor, but does not demonstrate the compound effectively preventing, reducing or delaying the onset of myelosuppression associated with cytotoxic chemotherapy or ionizing radiation therapy. As taught by Gomtsyan et al. and Terasaka, just because a compound inhibits adenosine does not mean that the compound is effective in treating all or any adenosine mediated disorder. Thus, one skilled in the art is not enabled from the Applicant's specification to effectively preventing, reducing or delaying the onset of myelosuppression associated with cytotoxic chemotherapy or ionizing radiation therapy because prior art teaches that adenosine inhibitors in general are not effective to treat adenosine-mediated disorders. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02.

(7) The quantity of experimentation necessary:

The instant claims read on preventing, reducing or delaying the onset of myelosuppression associated with cytotoxic chemotherapy or ionizing radiation therapy.

As discussed above the specification fails to provide any support for effectively preventing, reducing or delaying the onset of myelosuppression associated with cytotoxic chemotherapy or ionizing radiation therapy. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F. 3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable. One skilled in the art would need to first establish that the Applicant's claimed compounds is actually effective in preventing, reducing or delaying the onset of myelosuppression associated with cytotoxic chemotherapy or ionizing radiation therapy.

In conclusion, the applicant is enabled for inhibiting binding at the adenosine receptor with the claimed compound, but not for preventing, reducing or delaying the onset of myelosuppression associated with cytotoxic chemotherapy or ionizing radiation therapy.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KENDRA D. CARTER whose telephone number is (571)272-9034. The examiner can normally be reached on 7:30 am - 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/K. D. C./
Examiner, Art Unit 1617

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617